REMARKS

In this Amendment, claim 3 has been canceled. Therefore, after entry of this Amendment which is respectfully requested, claims 1, 2, and 4-6 will be all the claims pending in the Application.

Initially, Applicants note that the Examiner did not initial Ikuyama et al. (1998) on the PTO Form-1449, submitted with Applicants' Information Disclosure Statement of April 19, 2002. Applicants respectfully request that the Examiner initial the Ikuyama reference to indicate that the reference has been considered. A copy of the Form-1449 as well as a copy of Ikuyama et al. (1998) are attached to this Response for the Examiner's convenience.

I. Objections to the Specification and Claim Rejections Under 35 U.S.C. § 112

At page 2 of the Office Action, the Examiner objects to the specification and rejects claims 1-6, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description and enablement requirements. Specifically, the Examiner states that the KGN cells are required to practice the claimed invention, and therefore, must be readily available to the public or obtainable by a repeatable method set forth in the specification. The Examiner further states that since the specification does not describe such a method, the KGN cells must be deposited. The Examiner states that if the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration establishing such will be sufficient to overcome the rejection.

Applicants submit that the KGN cells have been deposited under the terms of the Budapest Treaty, as indicated by the deposit receipt submitted to the Patent Office with Applicants' Preliminary Amendment filed December 4, 2002. In addition, Applicants submit that the Preliminary Amendment of December 4, 2002 amended the specification to include the KGN cell line deposit information at page 12, lines 3-4. Further, Applicants now provide the attached Statement of Availability further establishing that the KGN cell line was deposited under the terms of the Budapest Treaty.

In view of the above, Applicants respectfully request that the objection to the specification and rejections of claims 1-6 under 35 U.S.C. § 112, be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 102

(1) At page 4 of the Office Action, the Examiner rejects claims 1-6 under 35 U.S.C. § 102(a) as anticipated by Saitoh et al. (November 23, 2001). Specifically, the Examiner states that Saitoh teaches detecting aromatase activity in KGN cells upon addition of tributytin and triphenyltin. The Examiner further states that Saithoh detects aromatase activity by $[^3H]H_2O$ release upon conversion of [1β-^{3}H]androstenedione to estrone, and by RIA.

Applicants submit that the present inventors are co-authors of Saitoh et al. (November 23, 2001). Further, Applicants submit, and as set forth in the attached Declaration Under 37 C.F.R. § 1.132, that the present inventors are the only inventors of claims 1-6, and that the remaining co-authors of Saitoh et al. were acting solely at the direction of the present inventors.

Accordingly, Saitoh et al. (November, 2001) is not 102(a) prior art against the present claims and Applicants respectfully request that this rejection be withdrawn.

(2) At page 5 of the Office Action, the Examiner rejects claims 1-6 under 35 U.S.C. § 102(a) as anticipated by Nishi et al. (January, 2001). Specifically, the Examiner states that Nishi teaches that the aromatase activity of KGN cells is stimulated by $(Bu)_2$cAMP or FSH. The Examiner further states that Nishi teaches detection of aromatase activity by $[^3H]H_2O$ release upon conversion of [1β-^{3}H]androstenedione to estrone, and by RIA.

Applicants submit that the present inventors are co-authors of Nishi et al. (January 2001). Further, Applicants submit, and as set forth in the attached Declaration Under 37 C.F.R. § 1.132, that the present inventors are the only inventors of claims 1-6, and that the remaining co-authors of Nishi et al. (January, 2001) were acting solely at the direction of the present inventors.

Accordingly, Nishi (January, 2001) is not 102(a) prior art against the present claims and Applicants respectfully request that this rejection be withdrawn.

(3) At page 5 of the Office Action, the Examiner rejects claims 1-6 under 35 U.S.C. § 102(a) as anticipated by Mu et al. (January, 2001). Specifically, the Examiner states that Mu teaches that the aromatase activity of human granulosa cells is inhibited by Troglitizone (TGZ) and the RXR specific ligand LG100268. The Examiner further states that Mu teaches detection of aromatase activity by $[^3H]H_2O$ release upon conversion of [1β-^{3}H]androstenedione to estrone, and by RIA.

Applicants submit that the present inventors are co-authors of Mu et al. (January, 2001). Further, Applicants submit, and as set forth in the attached Declaration Under 37 C.F.R. § 1.132, that the present inventors are the only inventors of claims 1-6, and that the remaining co-authors of Mu et al. (January, 2001) were acting solely at the direction of the present inventors.

Accordingly, Mu (January, 2001) is not 102(a) prior art against the present claims and Applicants respectfully request that this rejection be withdrawn.

(4) At page 5 of the Office Action, the Examiner rejects claims 1-6 under 35 U.S.C. § 102(b) as anticipated by Mu et al. (2000). Specifically, the Examiner states that Mu (2000) teaches that the aromatase activity of human granulosa cells is inhibited by Troglitizone (Tro) and the RXR specific ligand LG100268. The Examiner further states that Mu (2000) teaches detection of aromatase activity by $[^3H]H_2O$ release upon conversion of $[1\beta\text{-}^3H]$ androstenedione to estrone, and by RIA.

Applicants respectfully submit that, with regard to claims 3, 4 and 5, that Mu (2000) does not anticipate these claims because Mu (2000) does not assay with the KGN or comparable tumor cell line. With regard to claims 1, 2, and 6, amended independent claim 1 recites "a granulosa-like tumor cell-line," after incorporation of claim 3 which has now been canceled. Applicants submit that since Mu (2000) uses only primary cultures prepared via *in vitro* fertilization to assay for aromatase activity, and that Mu (2000) does not teach or suggest the method of identifying an endocrine disruptor with a "granulose-like tumor cell line."

Accordingly, Applicants respectfully request that this rejection be withdrawn.

(5) At page 6 of the Office Action, the Examiner rejects claims 1-2 and 6 under 35 U.S.C. § 102(b) as anticipated by Nawata (1995). Specifically, the Examiner states that Nawata teaches that the activity of aromatase in human osteoblast-like cells is stimulated by dexamethasone and 1α- 25-dihyroxyvitamin D. Claim 3, which has been incorporated into claim 1, is not rejected as anticipated by Nawata.

Applicants assert that Nawata does not show aromatase activity of a granulosa-like cell line, but an osteoblast-like cell line. Thus, Applicants submit that Nawata does not teach or suggest the method of identifying an endocrine disruptor using a granulosa-like tumor cell line as claimed.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

(6) At page 6 of the Office Action, the Examiner rejects claims 1 and 6 under 35 U.S.C. § 102(b) as anticipated by Zacharewski (1998). Specifically, the Examiner states that Zacharewski teaches that it had been known that aromatase activity could be inhibited in porcine granulosa cells by 4-hydroxyandrostendione, aminoglutethimide phosphate, and ketoconazole. Claim 3, which has been incorporated into claim 1, is not rejected as anticipated by Zacharewski.

Applicants assert that amended claim 1 recites a "granulosa-like tumor cell line." As the Examiner does not contend that Zacharewski teaches or suggests a granulosa-like tumor cell line, Applicants respectfully request that this rejection be withdrawn.

(7) At page 6 of the Office Action, the Examiner rejects claims 1 and 6 under 35 U.S.C. § 102(b) as anticipated by Mak (1999). Specifically, the Examiner states that Mak teaches a yeast screening system for aromatase inhibitors, and Mak detects aromatase activity by $[^3H]H_2O$ release upon conversion of $[1\beta\text{-}^3H]$androstenedione to estrone. Claim 3, which is now incorporated into claim 1, is not rejected as anticipated by Zacharewski.

Applicants submit that Mak does not teach a granulosa-like tumor cell line with aromatase activity, and accordingly, Mak does not teach or suggest a method of identifying an endocrine disruptor using a granulosa-like tumor cell line.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

(8) At page 6 of the Office Action, the Examiner rejects claims 1 and 6 under 35 U.S.C. § 102(b) as anticipated by Kitawaki (1993) and Chen (1999). Specifically, the Examiner states that both Kitwaki and Chen use MCF-7 human breast cancer cells to screen for inhibitors of aromatase. Claim 3, which is now incorporated into claim 1, is not rejected as anticipated by Kitawaki or Chen.

Applicants submit that neither Kitawaki nor Chen teach an aromatase assay using a granulosa-like tumor cell line as recited in amended claim 1, and accordingly, neither Kitawaki nor Chen teach or suggest a method of identifying an endocrine disruptor using a granulosa-like tumor cell line.

Accordingly, Applicants respectfully request withdrawal of this rejection.

(9) At page 7 of the Office Action, the Examiner rejects claims 1 and 6 under 35 U.S.C. § 102(b) as anticipated by Powlin (1998). Specifically, the Examiner states that Powlin teaches screening for aromatase inhibitors with testis and ovary explants. Claim 3, which is now incorporated into claim 1, is not rejected as anticipated by Powlin.

Applicants submit that Powlin does not teach the aromatase assay with a granulosa-like tumor cell-line, as recited in amended claim 1, and accordingly, Powlin does not teach or suggest a method of identifying an endocrine disruptor using a granulosa-like tumor cell line.

Accordingly, Applicants respectfully request withdrawal of this rejection.

(10) At page 7 of the Office Action, the Examiner rejects claims 1-2 and 6 under 35 U.S.C. § 102(b) as anticipated by Tanaka (1995). Specifically, the Examiner states that

Tanaka teaches activating aromatase activity in human osteoblast-like osteosarcoma cells with dexamethazone and other glucocoriticoids. Claim 3, which has been incorporated into claim 1, is not rejected as anticipated by Tanaka.

Applicants submit that the cell line of Tanaka is not a granulosa-like tumor cell line as recited in amended claim 1. Thus, Tanaka does not teach or suggest a method of identifying an endocrine disruptor using a granulosa-like tumor cell line.

Accordingly, Applicants respectfully request withdrawal of this rejections.

III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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